Remarks

Claims 1, 2, 4-7, 9, 10, 12 and 13 are pending. Claims 1 and 13 have been amended to more clearly claim what the Applicant considers to be his invention. Claims 3, 8 and 11 have been cancelled.

Rejection Under 35 U.S.C. § 112

Claims 1, 2, 4-7, 9, 10, 12 and 13 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, based on the recitation "administered about simultaneously".

Claim 1 has been amended to recite "...comprising administering antibodies to Her-2/neu receptor and at least one chemotherapeutic agent in conjunction with radiation therapy." Applicants submit that the administration step can be precisely determined by those of skill in the art. As such, Applicant respectfully submits that the rejection of claims, 2, 4-7, 9, 10, 12 and 13 under 35 U.S.C. § 112, first paragraph is moot and respectfully request withdrawal of this rejection.

Claims 1, 2, 4-7, 9, 10, 12 and 13 have also been rejected under 35 U.S.C. 112, second paragraph. The Examiner alleges that the language of Claim 13 broadens the scope of the antibodies to be administered. Claim 13 has been amended to recite wherein the antibodies to a Her-2/neu receptor are administered at a higher dosage at the first dose than at a subsequent dose. Applicant submits that newly amended claim 13 no longer broadens the scope of the antibodies to be administered. As such, Applicant respectfully submits that the rejection of

claims, 2, 4-7, 9, 10, 12 and 13 under 35 U.S.C. § 112, first paragraph is moot and respectfully request withdrawal of this rejection.

Rejection Under 35 U.S.C. § 102

1. Claims 1, 2, 4-7, 9, 10, 12 and 13 were rejected under 35 U.S.C. § 102(e), as being anticipated by U.S. Patent number 6,632,979 B2 (hereinafter referred to as "the '979 patent"). Applicant respectfully traverses this rejection.

In making a rejection under 35 U.S.C. § 102, the Patent Office is burdened with establishing that the cited art teaches each and every limitation of the claims. The present rejection does not meet this burden. The present rejection fails to establish that the cited art teaches each and every limitation of the claims. The '979 patent does not disclose what is alleged in the Office Action and does not disclose what is presently claimed. As a result, the '979 patent fails to disclose every feature of the present claims. This error renders the rejection legally flawed with the result that the Office Action fails to establish a prima facie case of anticipation.

The '979 patent discloses a HER-2 transgenic mouse tumor mouse model that expresses HER2 at high levels, but poorly responds to HERCEPTIN®. (See Col. 1, lines 8-11). In addition, the '979 patent discloses methods to identify drug candidates to treat cancer.

The passages of the '979 patent cited in the Office Action fail to disclose method of inhibiting tumor growth in tumors having growth factor receptors comprising administering antibodies to Her-2/neu receptor and at least one chemotherapeutic agent in conjunction with radiation therapy.

Claims 1, 2, 4-7, 9, 10, 12 and 13 are drawn to a method of inhibiting tumor growth in tumors having growth factor receptors comprising administering antibodies to Her-2/neu receptor and at least one chemotherapeutic agent in conjunction with radiation therapy. (*Emphasis ours*). (See claim 1, lines 1-3).

The Office Action fails to address radiation therapy as part of the method. None of the portions of the '979 patent cited by the Examiner refer to or disclose using the antibodies disclosed therein with chemotherapeutic agents and radiation therapy. (*Emphasis ours*). The Office Action cites column 10, lines 59-65; column 26, line 53-column 27, line 2 which discloses therapeutic regimens combined with the coadministration of anti-cancer agents, such as HERCEPTIN® with chemotherapeutic agents. This is not the same as the claimed method. As described above, the claimed method is a method of inhibiting tumor growth in tumors having growth factor receptors comprising administering antibodies to Her-2/neu receptor and at least one chemotherapeutic agent in conjunction with radiation therapy. As such, the cited passages of the '979 patent fails to disclose a method of inhibiting tumor growth in tumors having growth factor receptors comprising administering antibodies to Her-2/neu receptor and at least one chemotherapeutic agent in conjunction with radiation therapy. Because the '979 patent fails to disclose every feature of the claimed compositions and because the present rejection fails to establish that the cited art teaches each and every limitation of the claims, the '979 patent fails to anticipate claims 1, 2, 4-7, 9, 10, 12 and 13.

2. Claims 1, 2, 4-7, 9, 10, 12 and 13 were rejected under 35 U.S.C. § 102(b), as being anticipated by U.S. Patent Application Publication number 2002/0051785 (hereinafter referred to as "the '785 application"). Applicant respectfully traverses this rejection.

For a prior art reference to anticipate a claimed invention, each and every element of the claimed invention must be disclosed in that single reference. Further, the disclosure in that single reference must be enabling. If one element of the claimed invention is not disclosed in the prior art reference, there is no anticipation. It is settled law that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently." *Verdegaal v. Union Oil*, 814 F2d. 628, 2 U.S.P.Q.2d 1051 (Fed. Cir. 1987).

The '785 application discloses methods for obtaining genetic profiles of cancer cells in order to assess that status of cancer in an individual. (See paragraph 0008). The '785 application also discloses compositions which comprise an antibody capable of inhibiting Her-2/neu receptor function and/or a TGF-β family member to reduce tumor growth. (See paragraph 13). The '785 application does mention that other additional therapies may be employed in the methods.

The disclosure in the '785 application provides that "yet additional therapies may be employed in the methods." (*Emphasis ours*) (See paragraph 0135). Nowhere in the application is a combination therapy actually performed or precisely described. At most, there is a mere suggestion to use an antibody capable of inhibiting Her-2/neu receptor function and/or a TGF-β family member with a chemotherapeutic agent and/or radiation therapy. That is, the disclosure indicates that these therapies may be used, but provides nothing more than a generic recitation of basic chemotherapeutic agent and radiation therapy protocols commonly employed in the art. (See paragraph 139). What the Examiner fails to appreciate is that a combination therapy utilizing antibodies to Her-2/neu receptor and at least one chemotherapeutic agent in conjunction with radiation therapy was not commonly employed in the art at the time the '785 application was filed. Thus, the disclosure indicates that the '785 application did not have possession of the

specific methods as claimed by Applicants, nor would one of ordinary skill in the art discern such a method, as is recited in the present invention. As such, the '785 application is not enabling for its disclosure of a method of inhibiting tumor growth in tumors having growth factor receptors comprising administering antibodies to Her-2/neu receptor and at least one chemotherapeutic agent in conjunction with radiation therapy. Thus, the '785 application does not serve as a proper §102 reference against the claimed invention.

Because the '785 application fails to serve as a proper §102 reference against the claimed invention, the '785 application fails to anticipate claims 1, 2, 4-7, 9, 10, 12 and 13.

3. Claims 1, 2, 4-7, 9, 10, 12 and 13 were rejected under 35 U.S.C. § 102(b), as being anticipated by Colbern et al. Applicant respectfully traverses this rejection.

In making a rejection under 35 U.S.C. § 102, the Patent Office is burdened with establishing that the cited art teaches each and every limitation of the claims. The present rejection does not meet this burden. The present rejection fails to establish that the cited art teaches each and every limitation of the claims. Colbern et al. does not disclose what is alleged in the Office Action and does not disclose what is presently claimed. As a result, Colbern et al. fails to disclose every feature of the present claims. This error renders the rejection legally flawed with the result that the Office Action fails to establish a prima facie case of anticipation.

Colbern et al. discloses a combination therapy with HERCEPTIN® and chemotherapy agents, specifically liposomal cisplatin and PL-cisplatin. (See Abstract, lines 2-3 and page 120, Conclusions).

The passages of Colbern et al. cited in the Office Action fail to disclose method of inhibiting tumor growth in tumors having growth factor receptors comprising administering

antibodies to Her-2/neu receptor and at least one chemotherapeutic agent in conjunction with radiation therapy.

Claims 1, 2, 4-7, 9, 10, 12 and 13 are drawn to a method of inhibiting tumor growth in tumors having growth factor receptors comprising administering antibodies to Her-2/neu receptor and at least one chemotherapeutic agent in conjunction with radiation therapy. (*Emphasis ours*). (See claim 1, lines 1-3).

The Office Action fails to address radiation therapy as part of the method. None of the portions of Colbern et al. cited by the Examiner refer to or disclose using the antibodies disclosed therein with chemotherapeutic agents and radiation therapy. (*Emphasis ours*). The Office Action cites the Abstract, page 118, sections 2.3 and 2.5 and the Results section which discloses combination therapies with HERCEPTIN® and liposomal cisplatin and PL-cisplatin. This is not the same as the claimed method. As described above, the claimed method is a method of inhibiting tumor growth in tumors having growth factor receptors comprising administering antibodies to Her-2/neu receptor and at least one chemotherapeutic agent in conjunction with radiation therapy. As such, the cited passages of Colbern et al. fails to disclose a method of inhibiting tumor growth in tumors having growth factor receptors comprising administering antibodies to Her-2/neu receptor and at least one chemotherapeutic agent in conjunction with radiation therapy. Because Colbern et al. fails to disclose every feature of the claimed compositions and because the present rejection fails to establish that the cited art teaches each and every limitation of the claims, Colbern et al. fails to anticipate claims 1, 2, 4-7, 9, 10, 12 and 13.

Rejection Under 35 U.S.C. § 103

1. Claims 1, 2, 4-7, 9, 10, 12 and 13 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Application Publication number 2002/0051785 (hereinafter referred to as "the '785 application"), in view of U.S. Patent number 6,632,979 B2 (hereinafter referred to as "the '979 patent"). Applicants respectfully traverse this rejection.

In order for a reference or a combination of references to anticipate a claim or claims, "[f]irst, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP § 2143.

The standard for obviousness requires both a motivation to arrive at the claimed subject matter as well as a reasonable expectation of success that the claimed subject matter would work. A motivation to try is not sufficient. It is the burden of the Office to show that the prior art, when considered as a whole, teaches or suggests every element of Applicants' claims. Moreover, "There must be some motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant." *In re Kotzab*, 217 F.3d 1365, 1370 (Fed Cir. 2000). The suggestion or motivation asserted must also be supported by objective evidence, not mere conclusory assertions. *See In re Dembiczak*, 175 F.3d 994, 999 (Fed Cir. 1999). The prior art must also provide a reasonable expectation of success for the proposed combination. *See In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed Cir. 1988). *See* MPEP § 2143 ("The teaching or motivation to make the claimed combination and the reasonable expectation of success must

both be found in the prior art, not in applicant's disclosure.") (citing *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir.1991)).

Notably absent from the Office's rejection is the identification of a suggestion, teaching or motivation that would lead one of ordinary skill in the art to make the leap of logic to take steps to arrive at the present invention. It is not enough to combine cited references with unspecified knowledge in the art without some objective reason to do so. Rather, to make this combination without evidence of such knowledge or the suggestion, teaching or motivation to combine is an impermissible hindsight reconstruction and simply takes the inventor's disclosure as a blueprint for piecing together the prior art in an effort to defeat patentability. (See In re Dembiczak, 50 U.S.P.Q.2d 1614 (Fed. Cir.1999)). Simply put, the motivation to combine references can not come from the invention itself. (See In re Oetiker, 977 F.2d 1443, 1447, 24 USPQ2d 1443, 1446 (Fed. Cir.1992).

The rejection applies the '979 patent in the same way and for the same disclosure for which the '979 patent were applied in the rejection under 35 U.S.C. § 102. For at least the reasons discussed above in connection with the rejection under 35 U.S.C. § 102, the '979 patent fail to disclose or suggest every limitation of claims 1, 2, 4-7, 9, 10, 12 and 13. For example, the cited passages of the '979 patent fail to disclose or suggest a method of inhibiting tumor growth in tumors having growth factor receptors comprising administering antibodies to Her-2/neu receptor and at least one chemotherapeutic agent in conjunction with radiation therapy.

The disclosure in the '785 application provides that "yet additional therapies may be employed in the methods." (*Emphasis ours*) (See paragraph 0135). Nowhere in the application is a combination therapy actually performed or precisely described. At most, there is a mere

suggestion to use an antibody capable of inhibiting Her-2/neu receptor function and/or a TGF-β family member with a chemotherapeutic agent and/or radiation therapy. That is, the disclosure indicates that these therapies may be used, but provides nothing more than a generic recitation of basic chemotherapeutic agent and radiation therapy protocols commonly employed in the art. (See paragraph 139).

Applicant emphasizes that prior to Dr. Buchsbaum's work, methods of inhibiting tumor growth in tumors having growth factor receptors comprising administering antibodies to Her-2/neu receptor and at least one chemotherapeutic agent in conjunction with radiation therapy were unknown and not believed to be useful due to toxicity concerns. Certainly, there was no evidence that such a method would both prevent tumor growth and lead to a high regression rate. Prior to Dr. Buchsbaum's work, no one had performed such a method. Applicant again emphasizes that, prior to Dr. Buchsbaum's discovery, those in the field of oncology had behind them only mere wonders and suggestion of performing such a method and were aware of no reasonable prospects to solve the problem solved by Dr. Buchsbaum.

Regarding reasonable expectation of success, Applicant notes that there must have been a reasonable expectation of obtaining what is claimed, thus requiring that those in the art reasonably to **expect** the claimed method to work, not just that such a method might be possible. It is hindsight to say that such an expectation would have been present based on the present references. Applicant also notes that the Patent Office is burdened with showing that there was a reasonable expectation of success. This has not been done. Without a reasonable expectation of success, the present rejection cannot be maintained.

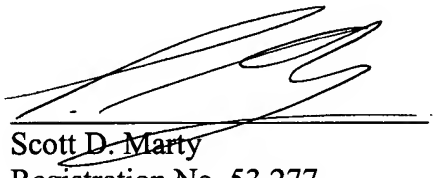
2. Claims 1, 2, 4-7, 9, 10, 12 and 13 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Colbern et al., in view of U.S. Patent number 6,632,979 B2 (hereinafter referred to as "the '979 patent"). Applicants respectfully traverse this rejection.

The rejection applies Colbern et al. and the '979 patent in the same way and for the same disclosure for which Colbern et al. and the '979 patent were applied in the rejection under 35 U.S.C. § 102. For at least the reasons discussed above in connection with the rejection under 35 U.S.C. § 102, Colbern et al. and the '979 patent fail to disclose or suggest every limitation of claims 1, 2, 4-7, 9, 10, 12 and 13. For example, the cited passages of Colbern et al. and the '979 patent fail to disclose or suggest a method of inhibiting tumor growth in tumors having growth factor receptors comprising administering antibodies to Her-2/neu receptor and at least one chemotherapeutic agent in conjunction with radiation therapy. Thus, Colbern et al. and the '979 patent, either alone or in combination, fail to disclose or suggest each and every element of claims 1, 2, 4-7, 9, 10, 12 and 13.

A Credit Card Payment Form PTO-2038 authorizing payment in the amount of $510.00, $510.00 representing the fee for a small entity under 37 C.F.R. § 1.17(a)(3), and a Request for Three Month Extension of Time are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

NEEDLE & ROSENBERG, P.C.



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